PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 924-	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/IL2004/000920	International filing date *(day/month/year)* 05.10.2004	Priority date *(day/month/year)* 07.10.2003

International Patent Classification (IPC) or national classification and IPC
C07K16/40, A61K39/395, A61P37/00

Applicant
YEDA RESEARCH AND DEVELOPMENT CO. LTD.

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
19.04.2005	17.02.2006

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/IL2004/000920

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-76 as originally filed

Sequence listings part of the description, Pages

1-6 as originally filed

Claims, Numbers

1-63 as originally filed

Drawings, Figures

1-7 as originally filed

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 26-30,52-59

because:

☒ the said international application, or the said claims Nos. 26-30,52-59 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-11,14-25,31-44,46-51,60-63
	No:	Claims	1,12,13,45
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-25,31-51,60-63
Industrial applicability (IA)	Yes:	Claims	1-25,31-51,60-63
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment on

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional observations, if necessary:

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 26-30,52-59 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT)and no examination with regard to novelty and inventive step is performed (Art. 33(1) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: "Phospho specific Antibodies" NACALAI TESQUE NEWS, vol. 12, 2001, XP002315815 Retrieved from the Internet: URL:http://www.nacalai.co.jp/catalog/PDF/n o12.pdf> [retrieved on 2005-01-28]

D2: EP-A-1 201 765 (AXXIMA PHARMACEUTICALS AKTIENGESELLSCHAFT) 2 May 2002 (2002-05-02)

D3: WO 97/37016 A1 (YEDA RESEARCH AND DEVELOPMENT CO. LTD; WALLACH, DAVID; MALININ, NIKOLA) 9 October 1997 (1997-10-09)

D4: LIN X ET AL: "MOLECULAR DETERMINANTS OF NF-KAPPAB-INDUCING KINASE ACTION" MOLECULAR AND CELLULAR BIOLOGY, AMERICAN SOCIETY FOR MICROBIOLOGY, WASHINGTON, US, vol. 18, no. 10, October 1998 (1998-10), pages 5899-5907, XP002920401 ISSN: 0270-7306

1 Novelty (Art. 33(2) PCT)

1.1 The document D1 discloses (the references in parentheses applying to this document): a catalog concerning antibodies specifically recognizing NF kappa B inducing kinase (NIK) with a phosphorylated Thr 559 residue (p. 3, lower table). It is also clear

from the same table that this antibody is useful for several immunological assays such as westernblotting and immunohistochemistry. Therefore it is concluded that in view of D1 the subject-matter of independent claims 1,12,45 is not new in the sense of Article 33(2) PCT.

1.2 Claim 1 is broadly directed to all antibodies recognizing NIK or a fragment of NIK with a phosphorylated threonyl residue at position 559. It is well known that this represents the normal, active form of NIK (see D4 for info). Therefore any antibody specifically recognizing NIK in biological mixtures falls under the scope of claim 1. D2 discloses antibodies to a fragment of NIK which was able to detect NIK in western blot expression analysis. (example 8). Therefore the subject-matter of claim 1 is not new over D2 (Art. 33(2) PCT).

1.3 Independent claim 13 concerns a hybridoma clone characterised only by reference to its deposit number. However, the deposit number itself is not sufficient to distinguish this hybridoma from anyother hybridoma. Therefore the subject-matter of this claim is not novel (art. 33(2) PCT).

2 Inventive Step (Article 33(3) PCT)

2.1 In the light of the novelty discussion of the claims above and in the light of the description of the present application (notably the examples and figures), claim 11 seems of particular interest. Therefore the presence of inventive step is assessed for this claim: D1, discussed above, discloses antibodies against Thr-559-phosphorylated NIK. The difference between claim 11 and D1 is the fact that the antibodies are monoclonal. The advantages of monoclonal antibodies are obvious to the person skilled in the art. He would therefore without applying inventive skill set out to modify the prior art relating to polyclonal antibodies against phosphorylated NIK and arrive at the monoclonal antibodies of claim 11. It is not indicated anywhere in the application that there was a special technical obstacle to overcome or an unexpected effect associated with the solution of the present application. Therefore it is cloncluded that the subject-matter of independent claim 13 lacks inventive step (Article 33(3) PCT).

It is noted that the applicant investigated the properties of the antibodies cited in D1 (p. 8, lines 3-7 of the present application). However, contrary to the applicants statement, the catalog number seems still to be available up till the data of establishment of the International search report. Moreover, the applicant fails to provide compelling evidence for differences with the prior art that could form the basis of acknowledging inventive step (Art. 33(3) PCT).

2.2 Independent claims 14,31,37,47,60,62,63 refer to subject-matter which with regard to inventive step, are dependent on the presence of inventive step of the NIK antibody. In the light of D1 as discussed above, these claims can therefore not be considered as inventive.

2.3

Dependent claims 2-11,15-25,32-36,38-44,46,48-51,61 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step, see documents D1-D4 and the corresponding passages cited in the search report.